Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Tenofovir Alafenamide (Vemlidy, TAF)

(Last updated December 24, 2019; last reviewed December 24, 2019)

Animal Studies

Carcinogenicity

Because tenofovir alafenamide (TAF) is rapidly converted to tenofovir (TFV), and TFV exposure in rats and mice is lower after TAF administration than after tenofovir disoproxil fumarate (TDF) administration, carcinogenicity studies were performed with TDF. Long-term oral carcinogenicity studies of TFV in mice and rats were carried out at TFV exposures that were 167 times (in mice) and 55 times (in rats) the exposures observed in humans who received the recommended doses of TAF. In female mice, liver adenomas were increased. TAF showed no evidence of carcinogenic activity in rats.[1,2]

Reproduction/Fertility

Reproduction studies have been performed at TAF exposures that were similar to (in rats) and 53 times higher than (in rabbits) the exposure seen in humans who received the recommended dose. These studies revealed no evidence of impaired fertility or mating performance associated with TAF administration.[1,2]

Teratogenicity/Adverse Pregnancy Outcomes

No effects on early embryonic development were seen when TAF was administered to male or female rats at doses that produced exposures that were 62 times the exposure seen in humans who received the therapeutic dose.[1,2]

Placental and Breast Milk Passage

Rat studies demonstrated secretion of TFV in breast milk after administration of TDF; whether TAF is present in animal milk is unknown.[1]

Human Studies in Pregnancy

Pharmacokinetics

The pharmacokinetics (PKs) of TAF were evaluated in 31 women who were taking TAF 25 mg without a PK enhancer, and in 27 women who were taking TAF 10 mg boosted with cobicistat (COBI) 150 mg.[3] This study evaluated plasma TAF exposures with and without boosting in pregnant and postpartum women relative to those in nonpregnant adults. No significant differences in PKs were seen between pregnant and postpartum women who were taking TAF 10 mg boosted with COBI. Pregnant women who were taking unboosted TAF had plasma TAF exposures that were similar to those observed in nonpregnant adults. During the postpartum period, however, TAF exposures in these women increased significantly. Another report described TAF PKs in 17 women who were taking TAF 25 mg boosted with either COBI or ritonavir. Plasma exposures for TAF during pregnancy were similar to those seen during the postpartum period.[4]

Placental and Breast Milk Passage

TAF was below the assay limit of quantification (<3.9 ng/mL) in 15 of 15 cord blood samples tested.[3] Intracellular TFV diphosphate was not measured in the cord blood or the samples of maternal plasma at delivery. Maternal plasma TAF concentrations at delivery were measurable in two of the 15 paired samples. No data are available on the breast milk passage of TAF in humans.

Teratogenicity/Adverse Pregnancy Outcomes

In the Antiretroviral Pregnancy Registry, the number of reported cases of TAF exposures is insufficient to draw any conclusions about the risk of birth defects.[5]

Excerpt from Table 8

Note: When using FDC tablets, refer to other sections in Appendix B and Table 8 for information about the dosing and safety of the individual drug components of the FDC tablet during pregnancy.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations[a]	Use in Pregnancy
Tenofovir Alafenamide (TAF) *Vemlidy* (TAF/BIC/FTC) *Biktarvy* (TAF/FTC) *Descovy* (TAF/EVG/c/FTC) *Genvoya* (TAF/FTC/RPV) *Odefsey* (TAF/DRV/c/FTC) *Symtuza*	**TAF (Vemlidy)** *Tablet:* • 25 mg **TAF/BIC/FTC (Biktarvy):** • TAF 25 mg/BIC 50 mg/FTC 200 mg tablet **TAF/FTC (Descovy):** • TAF 25 mg/FTC 200 mg tablet **TAF/EVG/c/FTC (Genvoya):** • TAF 10 mg/EVG 150 mg/COBI 150 mg/FTC 200 mg tablet **TAF/FTC/RPV (Odefsey):** • TAF 25 mg/FTC 200 mg/RPV 25 mg tablet **TAF/DRV/c/FTC (Symtuza):** • TAF 10 mg/DRV 800 mg/COBI 150 mg/FTC 200 mg tablet	**Standard Adult Doses** *TAF (Vemlidy):* • One tablet once daily with food *TAF/BIC/FTC (Biktarvy):* • One tablet once daily with or without food *TAF/FTC (Descovy):* • One tablet once daily with or without food • Same dose (TAF 25 mg) can be used with or without PK enhancers. *TAF/EVG/c/FTC (Genvoya):* • One tablet once daily with food *TAF/FTC/RPV (Odefsey):* • One tablet once daily with food *TAF/DRV/c/FTC (Symtuza):* • One tablet once daily with food **Pregnancy** *PKs in Pregnancy:* • Plasma PKs not significantly altered in pregnancy. *Dosing in Pregnancy:* • No change in dose indicated. For guidance about the use of combination products in pregnancy, please see the specific sections on other components (i.e., BIC, COBI, DRV, EVG, FTC, RPV).	Low placental transfer to fetus.[b] Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats. Renal function should be monitored because of the potential for renal toxicity.

[a] Individual ARV drug doses may need to be adjusted in patients with renal or hepatic insufficiency (for details, see the Adult and Adolescent Antiretroviral Guidelines, Appendix B, Table 10).

[b] Placental transfer categories are determined by mean or median cord blood/maternal delivery plasma drug ratio:

High: >0.6 **Moderate:** 0.3–0.6 **Low:** <0.3

Key: ARV = antiretroviral; BIC = bictegravir; COBI = cobicistat; DRV/c = darunavir/cobicistat; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; PK = pharmacokinetic; RPV = rilpivirine; TAF = tenofovir alafenamide

References

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2. Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (Genvoya) [package insert]. Food and Drug Administration. 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/207561s023lbl.pdf.
3. Momper J, Best B, Wang J, et al. Tenofovir alafenamide pharmacokinetics with and without cobicistat in pregnancy. Presented at: 22nd International AIDS Conference. 2018. Amsterdam, Netherlands.
4. Brooks K, Pinilla M, Shapiro D, et al. Pharmacokinetics of tenofovir alafenamide 25 mg with PK boosters during pregnancy and postpartum. Presented at: Workshop on Clinical Pharmacology of HIV, Hepatitis, and Other Antiviral Drugs. 2019. Noordwijk, Netherlands.
5. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 January 2019. Wilmington, NC: Registry Coordinating Center. 2019. Available at: http://www.apregistry.com/.